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- (71) Applicant (for all designated States except US): ASTER-ION LIMITED [GB/GB]; Firth Court, Sheffield S10 2TN (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): ROSS, Richard [GB/GB]; Asterion Limited, Firth Court, Sheffield S10 2TN (GB). SAYERS, Jon [GB/GB]; Asterion Limited. Firth Court, Sheffield S10 2TN (GB). ARTYMIUK, Peter [GB/GB]; Asterion Limited, Firth Court, Sheffield S10 2TN (GB).
- HARRISON GODDARD FOOTE, 31 St. (74) Agent: Saviourgate, York YO1 8NQ (GB).

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(54) Title: CYTOKINE POLYPEPTIDES AND ANTIBODIES CONTAINING A SIGNAL SEQUENCE FOR THE ATTACHE-MENT OF GLYCOSYLPHOSPHATIDYLINOSITOL

(57) Abstract: The invention relates to chimerical recombinant polypeptides, preferably therapeutic polypeptides, for example cytokines or antibodies, which are engineered to include a signal sequence for the attachment of glycosylphosphatidylinositol; cells expressing said polypeptides and methods to manufacture said polypeptides.



**Application No** 

PCT/GB2004/001572 A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/19 C12N15/62 C07K14/52 C07K19/00 A61K38/19 A61K39/395 C07K16/00 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C12N C07K IPC 7 A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fleids searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data, EMBL C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X BENTING JUERGEN H ET AL: "N-glycans 1,2,6,7, mediate the apical sorting of a 34-40 GPI-anchored, raft-associated protein in Madin-Darby canine kidney cells" JOURNAL OF CELL BIOLOGY, vol. 146, no. 2, 26 July 1999 (1999-07-26), pages 313-320, XP002301129 ISSN: 0021-9525 abstract Υ 3-5. 8-18 25 - 33-/--Further documents are listed in the continuation of box C. X Patent family members are listed in annex. Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention "E" earlier document but published on or after the International \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-ments, such combination being obvious to a person skilled citation or other special reason (as specified) O' document referring to an oral disclosure, use, exhibition or other means \*P\* document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of malling of the international search report 0 7, 03, 05 26 October 2004 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni,

Fax: (+31-70) 340-3016

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Form PCT/ISA/210 (continuation of second sheet) (January 2004)

Application No
PCT/GB2004/001572

ation) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Relevant to claim No.
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	membrane protein and its interaction with thyrotrophin and autoantibodies" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 19, 8 May 1998 (1998-05-08), pages 11874-11880, XPO02246413 ISSN: 0021-9258 abstract figure 1  WO 96/34105 A (FASEL NICOLAS JOSEPH; REYMOND CHRISTOPHE DOMINIQUE (CH); RMF DICTAGEN) 31 October 1996 (1996-10-31) page 6, line 24 - line 31  US 6 136 563 A (OLSON KENNETH ET AL) 24 October 2000 (2000-10-24) cited in the application column 4, line 17 - line 60  WO 02/083851 A (GENVEC INC; KESSLER PAUL D (US); KOVESDI IMRE (US)) 24 October 2002 (2002-10-24) paragraph '0096! - paragraph '0099!  BROSTEDT P ET AL: "CHARACTERIZATION OF DIMERIC FORMS OF HUMAN PITUITARY GROWTH HORMONE BY BIOASSAY, RADIORECEPTOR ASSAY, AND RADIOIMMUNOASSAY" ACTA ENDOCRINOLOGICA, vol. 122, no. 2, 1 February 1990 (1990-02-01), pages 241-248, XPO00618626 ISSN: 0001-5598 abstract; table 2  GUADIZ GAYLE ET AL: "The carboxyl terminus of Pneumocystis carinii glycosylphosphatidylinositol signal sequence" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 40, 2 October 1998 (1998-10-O2), pages 26202-26209, XPO02301131 ISSN: 0021-9258 abstract

Application No
PCT/GB2004/001572

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to surbject matter not required to be searched by this Authority, namely:
Although claim 40 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.:
No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-8 (partially), 9-18 (completely), 25-40 (partially)
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-8 (partially), 9-18 (completely), 25-40 (partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to growth hormone.

2. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to leptin.

3. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to erythropoietin.

4. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to prolactin.

5. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to TNF.

6. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to an interleukin.

7. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to G-CSF.

8. claims: 1-8, 25-40 (all partially)

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to GM-CSF.

9. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to CNTF.

10. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to cardiotrophin-1.

11. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to LIF.

12. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to oncostatin M.

13. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to interferon.

14. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to a cytokine not covered by subjects 1-13.

15. claims: 1 (partially), 19-24 (completely), 25-40 (partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to an antibody.

# FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

16. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to a polypeptide which is not a ligand binding domain of a cytokine receptor and which is not covered by subjects 1-15.

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